REMARKS/ARGUMENTS

The claims have been amended for greater clarity in referring to the immune response and in defining alternative forms of the agent as discussed in further detail below. Claim 45 has also been amended to recite that the second agent is linked to a carrier that helps elicit an immune response to the second agent or is administered with an adjuvant that augments an immune response to the second agent. No amendments should be construed as acquiescence in any ground of rejection. Lack of comments on any of the Examiner's remarks should not be construed as acquiescence thereof. Applicants use the paragraph numbering of the office action in responding to the Examiner's comments.

¶4. Claims 71–76, 79-80 and 83–84 stand rejected for alleged lack of enablement for elimination of all risk of disease. Applicants maintain their position from the appeal brief on this issue.

¶5. Claims 41-42, 45, and 51-52 stand rejected under 35 USC § 102(e) as allegedly anticipated by Jensen, US 2002/0187157. This rejection was discussed at length in the appeal brief. In short, applicants pointed out that Jensen refers to a large genus of diseases including Alzheimer's disease and Parkinson's disease and a large genus of potentially therapeutic agents including Aβ and alpha-synuclein, but never discloses that the very same treatment for Alzheimer's disease (namely administration of Aβ) should also be given to patients suffering from or at known genetic risk of Parkinson's disease. In fact, Jensen does not refer to administration of Aβ and Parkinson's disease in the same sentence or even the same paragraph. Thus, insofar as one can determine what Jensen is proposing, it would appear more likely he is proposing that amyloidogenic diseases principally associated with peptides other than Aβ be treated not with Aβ, the major peptide associated with Alzheimer's disease, but with whatever peptide plays a comparable role in the disease in question.

The Examiner alleges paragraphs 177-181 of Jensen provide additional relevant disclosure. These paragraphs refer to treating Alzheimer's and various other diseases

characterized by amyloid deposits including Parkinson's disease, by down-regulating amyloid activity. However, this passage is silent as to the agent to be used in treating Parkinson's disease. Therefore, applicants' position as stated in the appeal brief is equally applicable to this passage as to the previously cited passages from Jensen.

6. Claims 41, 43-44, 71, 73 - 74 stand rejected under 35 USC § 112, second paragraph as allegedly indefinite. The Examiner alleges that the phrase induces an immune response is unclear as applied to antibodies, and claim 74 is unclear whether the antibody is administered with or as an alternative agent to the Aβ fragment. In reply, the initial recitation that the agent induces an immune response has been deleted, and an immune response is used only in connection with administration of peptides or fragments. The claims have been also amended to use Roman numerals (i) and (ii) to designate the alternative forms of agent encompassed by the claims. It should thus be clear that an "antibody to Aβ" does refer to an agent to be administered.

¶7. Claims 41, 43, 45, and 51-52 stand rejected under 35 USC § 102(e) as allegedly anticipated by Weksler (U.S. Patent Application Publication 2004/0197831. The Examiner cites particularly paragraphs 25-27 as allegedly teaching antibodies raised against Aß peptide, paragraph 33 as allegedly teaching a pharmaceutical composition containing an anti-amyloid antibody, and paragraph 38 as allegedly teaching to administer the pharmaceutical composition to treat a variant of diseases including Alzheimer's and Parkinson's disease.

Weksler is mainly directed to a diagnostic method in which low levels of antibodies to Aβ42 are alleged to be an indicator of Alzheimer's disease. Like Jensen, Weksler provides a long list of diseases characterized by amyloid deposits and a long list of peptides involved in such diseases (paragraphs 21, 38 and 22). Like Jensen, Weksler never explicitly says that Aβ or an antibody thereto can be used for treatment of Parkinson's disease much less provides an example to show any effect of such treatment on Parkinson's disease. Although paragraphs 25-27 may refer to making an antibody to Aβ, and paragraph 33 of Weksler may refer to incorporating an anti-amyloid antibody into a pharmaceuctical composition, Weksler and

the art using the term amyloid more broadly referring to not just amyloid formed from Aβ but from any of the numerous peptides listed in paragraph 22. Thus, paragraph 33 is not referring specifically to an antibody to Aβ but an antibody to a disparate genus of amyloid peptides. Paragraph 38 likewise refers to a disparate genus of diseases characterized by amyloid deposits. Thus, the combination of paragraphs 38 and 33 at best provides a genus of diseases and a genus of agents without direction as to specific combinations. Applicants remarks and the case law regarding Jensen are thus also applicable to Weksler. The Examiner is respectfully requested to reconsider the extensive discussion of the relevant case law from the appeal brief.

¶¶8-9. Claims 41-42, 45-46, 48, 51-55, 71-72, 75-76, 79-81 and 83 stand rejected as allegedly obvious over Jensen. The rejections stem from the alleged premise that Jensen teaches to administer Aβ to patients with Parkinson's disease. For the reasons explained in the appeal brief, in applicants' submission, no such teaching is present in Jensen.

With respect to claims 54, 55, and 79-84, which specify that the patient is free of Alzheimer's disease or a disease characterized by extracellular deposits (which includes Alzheimer's disease), patentability is further shown by an unexpected result. Even if a *prima facie* case is established under 35 USC § 103, if applicant produces rebuttal evidence of adequate weight, "the holding of prima facie obviousness, being but a legal inference from previously uncontradicted evidence, is dissipated." *Piasecki*, 223 USPQ at 788. Generally, a showing of unexpected advantage is sufficient to overcome an obviousness where the unexpected advantage has practical significance greater than a known, expected result. *In re Nolan*, 193 USPQ 641, 645 (CCPA 1977). Here, immunization with Aβ reduces alpha-synuclein deposits even in the absence of abnormal Aβ deposits (specification at paragraph 186 and Figs. 5 and 6). Although Aβ has been previously shown to reduce deposits of Aβ (see, e.g., US 6,787,144), there was no reason to expect it would reduce the deposits of a different protein alpha-synuclein particularly in patients lacking abnormal deposits of Aβ. Thus, immunization with Aβ serves to ameliorate the fundamental pathology (alpha synuclein deposits) of Parkinson's disease as distinct from merely reducing a peptide associated with Alzheimer's disease whose pathological role if any, in Parkinson's patients free of Alzheimer's disease was not known. This unexpected advantage in

reducing the fundamental pathology of a disease rather than a peptide of unclear role in disease is submitted to overcome a prima facie case of obviousness, although as discussed above, applicants' disagree that such a case has been established.

¶10. Claims 41-42, 44-46, 48, 51, 71-71, 74-76 and 79-84 stand rejected as allegedly obvious over Jensen in view of Frangione. Frangione is alleged to teach administering immunogenic fragment of alpha synuclein to Parkinson's disease patients. This rejection is traversed based at least on the distinctions over Jensen discussed above.

¶11. Claims 41, 43, 45, 51-52, 73 and 75 stand rejected as allegedly obvious over Weksler. The rejections stem from the alleged premise that Weksler teaches to administer Aβ to patients with Parkinson's disease. Applicants disagree for the reasons given in connection with the anticipation rejection.

¶12. The present claims stand rejected for obviousness-type double patenting over several patents claiming treatment of diseases characterized by amyloid deposits of Aβ. The Examiner alleges that the present claims are not distinct from the claims in the cited patents because the claims in the cited patents encompass the present claims.

In reply, it is respectfully submitted that the rejection is based merely on domination; that is, the claims of the cited patents encompass the present claims. Domination does not preclude, but is itself insufficient, for double patenting.

> Domination and double patenting should not be confused. They are two separate issues. One patent or application "dominates" a second patent or application when the first patent or application has a broad or generic claim which fully encompasses or reads on an invention defined in a narrower or more specific claim in another patent or application. Domination by itself, i.e., in the absence of statutory or nonstatutory double patenting grounds, cannot support a double patenting rejection. *In re Kaplan,* 789 F.2d 1574, 1577-78, 229 USPQ 678, 681 (Fed. Cir. 1986); and *In re Sarrett*, 327 F.2d 1005, 1014-15, 140 USPQ 474, 482 (CCPA 1964). However, the

presence of domination does not preclude double patenting. See, e.g., *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968).

MPEP § 804. II.

Here, treatment of Parkinson's disease is not an obvious species of treatment of diseases in general characterized by amyloid deposits of Aβ because unlike diseases such as Alzheimer's and Down's syndrome in which amyloid deposits of Aβ are the primary disease pathology, in Parkinson's disease, the primary pathology is deposits of alpha synuclein and the role of Aβ deposit, if present, in pathogenesis of Parkinson's disease is unclear.

For these reasons, it is submitted that the rejections based on obviousness-type double patenting should be withdrawn.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

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